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Dangerous Delinquents

The Most Lethal Viruses Can Disappear Quickly,
Like That of the 1918 Influenza Epidemic

By Joshua Lederberg

VIRUSES ARE the infectious particles which account for many diseases not yet curable with modern drugs—*hepatitis*, measles, influenza, polio, the common cold and some animal tumors. The continued mystery and importance of this last discovery was signaled last month by Dr. Peyton Rous's Nobel Prize 50 years after his pioneering work on the chicken sarcoma virus.

The virus particle is hard to distinguish from fundamental parts of the normal cell. We can think of a virus as a parasitic organism which has shed all the functions needed for independent existence. It has retained the essential genetic function of reproducing itself in the infected host cell, plus a few others with which it can dominate the host's biochemical machinery.

A virus should also make a protective skin to enwrap its genetic material, enabling it to escape from a ravished cell; to drift to another fresh one to begin a new cycle of growth.

The virus has no malevolence. That the host cell is sometimes destroyed is a mere byproduct of its evolved chemical individuality. In fact, because the virus must depend on the host's metabolism, a dead host is useless to it. The most lethal viruses are the delinquent deviants, retaining a more precarious foothold on life than other viruses which have learned how to work a long term equilibrium with their hosts.

The virulent influenza strain of the 1918 pandemic has disappeared from the earth with some millions of humans; common cold viruses of the same vintage are surely still with us. Viruses are then only incidentally virulent. Many are nearly silent for cell pathology, but might influence cell behavior in other ways—perhaps even constructively.

Science and Man

THE SAME DAY that Dr. Rous received his Nobel Prize in Stockholm, Nature magazine in London published an article by Dr. Stanford Rogers on constructive effects in man of silent tumor viruses. This work is a translation into animal biology of much previous work on bacteriophages, the viruses that attack bacteria.

We find clear evidence that some silent viruses carry unique genetic information. An example of this virogenic conversion is in the diphtheria bacillus, whose most individualistic quality is to make poisonous toxin, which, rather than the membranous growth in a child's throat, was the horror of the disease. To produce the toxin, a diphtheria bacillus must previously have inherited a certain kind of bacteriophage.

Working at Oak Ridge on a joint AEC-NIH cancer research program, Dr. Rogers has been examining a variety of tumor viruses of animals for similar phenomena. He has studied humans who have been exposed to and probably accidentally infected by the Shope virus. They show evidence of a virogenic conversion that produces a special form of a common enzyme, arginase.

This Shope virus, which causes tumors in rabbits, apparently is a harmless passenger in man. Only a laboratory test for arginase activity could tell whether the virus was present.

Dr. Rogers' finding is, however, a sudden leap from a laboratory abstraction to an issue of immense human significance. Infection by a virus is already one of the most profound modifications a human personality can suffer, but so far we have perceived this only as an unwanted disease, or more recently as a vaccination against it. If one virus can encode a new arginase in infected humans, we can surely find other harmless viruses which can encode for other constructive changes in human quality.

FOR EXAMPLE, Dr. Rogers points out how to cure a genetic disease, like phenylketonuria, which causes severe mental retardation. We would find a silent virus that encodes for the missing enzyme, phenylalanine hydroxylase. We would then infect the infant with this virus.

Our present knowledge of virus genetics and biochemistry supports even grander expectations—to breed viruses for calculated virogenic effects. Their genetic information content would supplement that already embodied in the human genes. However, the limitation in our knowledge of human biology and ethical purpose makes it difficult to perceive just which changes are truly constructive.

We have heard anxious talk about the application of molecular genetics to human affairs. We know a great deal about the genetic code, but grave technical obstacles still forbid direct intervention in human genes. Dr. Rogers' discovery is a sudden sidetrack around these obstacles.

To use an infectious virus for genetic engineering aggravates the fundamental moral problem, since people may be involuntarily exposed to infection either by mischance spread or by authoritarian design. In fact, we already conduct the forerunner of such experiments by wide dissemination of polio vaccines.

These live viruses have certainly spread from inoculated children to their playmates, giving a desired broadening of immunity to the disease. Subtler effects of such vaccines, for all we can tell, may already occur, as they doubtless do with the innumerable wild viruses to which we are constantly exposed.

What we now foresee is the more deliberate engineering of virus genes for calculated changes in aspects of human nature less obviously coupled to what we call disease.

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